Brain and Spine 4 (2024) 102740

Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Dural reconstruction with or without a bone graft of paranasal and anterior skullbase malignancies: Retrospective single-center analysis of 11 cases and review of literature

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ARTICLE INFO

Handling editor: W Peul

Keywords:
Skull base tumor
Resection
Dural repair
Complications
Technique

ABSTRACT

Introduction: The reconstruction of frontobasal defects following oncologic resections of paranasal and anterior skull base (ASB) malignancies remains challenging. Ineffective reconstruction could lead to cerebrospinal fluid leak, meningitis, and tension pneumocephalus.
Research question: Aim of this investigation was to analyse postoperative complication rates with or without bone graft for anterior skull base reconstruction.
Material and methods: In this retrospective study, we included patients following resection of paranasal and/or anterior skull base malignancies between October 2013 and December 2022. Complications were analysed with regards to the type of skull base reconstruction.
Results: Eleven patients were identified (2 female, 9 male, age (median, SD) 64 ± 14.1 years (range 38–81). There were nine cases of paranasal sinus and nasal cavity carcinomas and two cases of olfactory neuroblastomas. Overall survival was 22.5 ± 28 months (range: 5–78), progression free survival was 17.0 ± 20.3 months (range: 11–78). Bone skull base reconstruction using a split graft was performed in three cases. Postoperative complications requiring surgical intervention were seen in 33% (one tension pneumocephalus) of cases in the bone reconstruction group and 50% (three patients with cerebrospinal fluid leak, one infection) in the non-bone reconstruction group.
Discussion and conclusion: The structural reinforcement of structural bone chip grafting might provide additional support of the ASB and prevent CSF leakage or encephalocele. Especially in large (>10 cm^2) bone defects of advanced sinonasal malignancies extending into the middle cranial fossa, the full armamentarium of reconstruction possibilities should be considered.

1. Introduction

Malignant tumors invading the anterior skull base (ASB), midface and sinonasal cavities are extremely rare with an incidence of approximately 0.6–0.8 per 100.000 population per year (Albonette-Felcio et al., 2020; Marinelli et al., 2018). They account for 3–6% of malignancies of the head & neck region (Turner and Reh, 2012; Dutta et al., 2015). The variety of histological subtypes and cell lines, rampant tumor growth and the complex anatomy of the affected structures require a multidisciplinary, highly specialized treatment. One cornerstone of current surgical therapy is a combination of endonasal, endoscopic and open transcranial/craniofacial techniques to maximize the extent of tumor mass reduction (Eloy et al., 2017).

The choice of surgical technique and graft materials are used vary considerably between the institutions. Primary goal is a water-tight dural closure separating the extracranial, upper respiratory tract from the intracranial space and to remodel structural defects. Craniofacial approaches include free autologous or allogeneic grafts, vascularized

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https://doi.org/10.1016/j.bas.2023.102740
Received 9 June 2023; Received in revised form 12 December 2023; Accepted 28 December 2023
Available online 30 December 2023

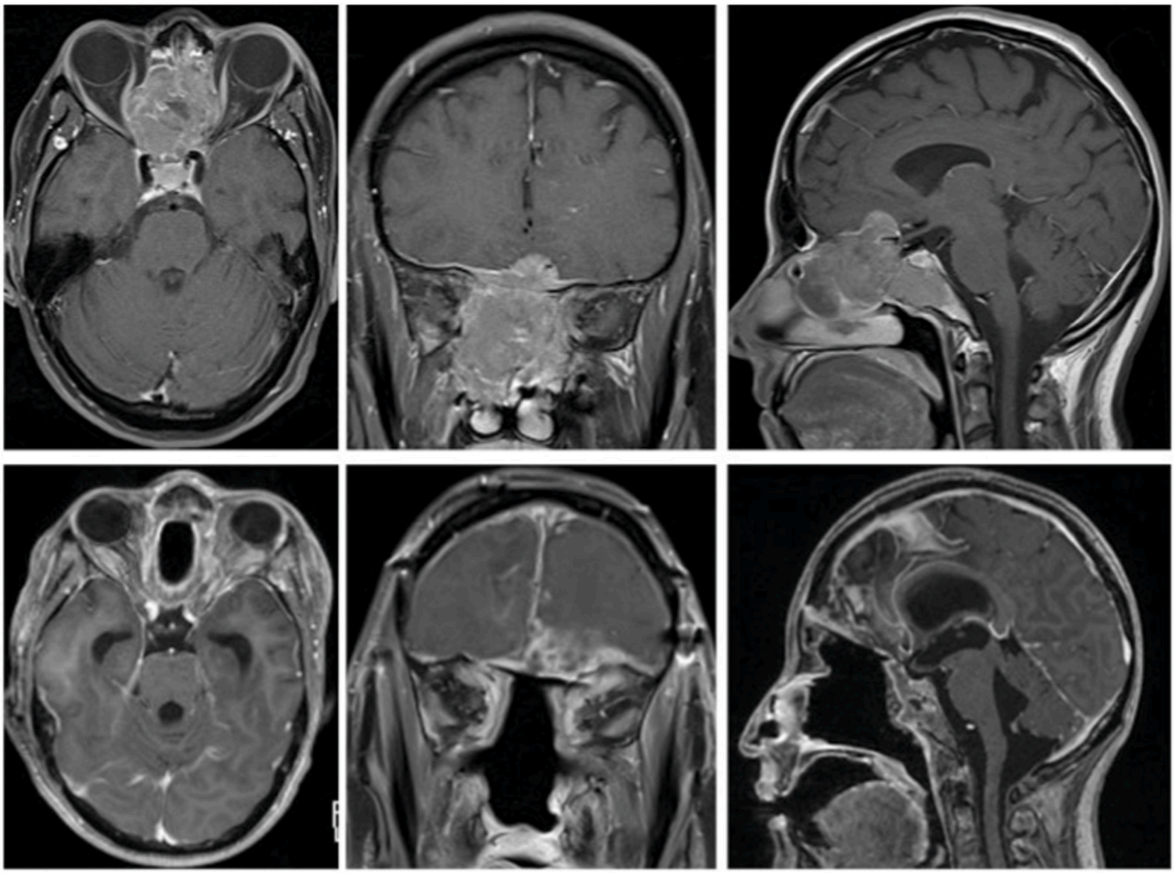

Fig. 1. Pre- (top row) and postoperative (bottom row) MRI scans (transversal, coronal, axial) with Gadolinium-DTPA contrast agent depicting the sinonasal and frontobasal esthesioneuroblastoma involving the middle cranial fossa (anterior clinoid process, chiasmatic groove) of patient No. 10. Residual tumor mass can be seen in the left superior part of the periorbita.

pedicled nasoseptal or pericranial flaps (Eloy et al., 2017), or free flaps (e.g. radial forearm, latissimus dorsi) (Ryan et al., 2023; Bohoun et al., 2019). Insufficient reconstruction can lead to life-threatening complications such as cerebrospinal fluid (CSF) leak, meningitis, intracranial abscess, or tension pneumocephalus (Sokoya et al., 2017; Kwon et al., 2012; He et al., 2021).

Depending on the size of the defect, especially when it involves a large portion of the cribriform plate and extending from the posterior table of the frontal sinus to the tuberculum sellae, rates of developing an encephalocele or CSF leak increase significantly (Moon et al., 2019). Here, rigid structural grafting using cartilage, bone or titanium mesh are discussed controversially regarding reabsorption and potential risk of infection (Eloy et al., 2017; Reinard et al., 2015; Yeung et al., 2021).

2. Theory

As no gold standard regarding surgical closure of large anterior skull base defects exists, we evaluated the outcome and complication rates after anterior skull base reconstruction with or without bone graft in our departments in the context of current literature.

3. Materials and Methods

We conducted a retrospective study and screened patient databases of the Departments of Neurosurgery and Otolaryngology, Head and Neck Surgery in a 9-year period between 2013 and 2022. Inclusion criteria were a) carcinoma of the sinonasal cavity invading the anterior skull base and extending intracranially, b) interdisciplinary surgery in a one-stage setting, and c) skull base reconstruction with or without bone graft. Exclusion criteria were a) meningeoma, osteoblastoma, schwannoma, melanoma, pseudotumors, b) biopsy only, c) pregnancy, d) age <18 and >80 years. The responsible local ethics committee of the Ludwig-Maximilians-University Munich had no ethical concerns regarding this study (written request on January 10th, 2022, personal communication). This retrospective study is in accordance with ethical principles for medical research involving human subjects as mentioned in the World Medical Association Declaration of Helsinki.

We obtained demographic data (age, sex), histological diagnosis, anatomical localization, numbers of previous surgeries, time to combined surgery, Karnofsky performance status (pre/post surgery), adjuvant radio-/chemotherapy, progression-free survival (PFS), overall survival (OS), completeness of resection according to early postoperative MRI scans, mortality, and surgery-associated early and late complications. Descriptive statistics (median, 1 standard deviation) are provided. Due to the small sample size, no statistical test was performed.

3.1. Radiological features

Every patient had CT, CT-angiography, and MRI with and without contrast agent (gadolinium DPTA) for preoperative planning. Pre- and postoperative tumor volume (MRI T1 MPRAGE) as well as the size of the bony defect after resection was calculated using the software of our navigation system (Brainlab Elements®, Brainlab AG, Munich, Germany).

3.2. Operative techniques

Two surgical techniques for malignant ASB tumors were used in a

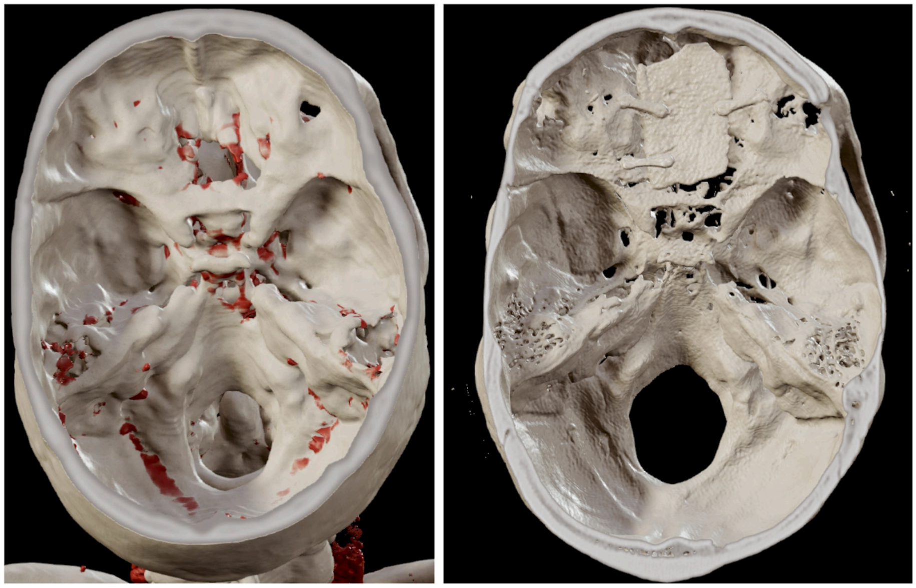

Fig. 2. Pre- (Fig. 2 **A**) and postoperative (Fig. 2 **B**) CT scans showing a 3D-reconstruction of the frontobasal bone defect (size 12.3 cm^2) of patient No. 10, which was covered with an autologous tabula externa bone chip.

Fig. 3. Virtual visualization of the tumor mass (red) and the implanted bone chip (orange).

single-stage setting. In every case, the operation was performed with a combined endonasal-endoscopic resection of tumor mass by our otolaryngology surgeons. After resection of the ethmoid bone and parts of the tumor-invaded superior and middle turbinates, the resection is extended to the sphenoid sinus, removing the rhinobasis and the vomer. If the tumor mass invaded the orbita, an orbital exenteration was performed. Then, the neurosurgical team joined in and continued the operation via a transfrontal approach. After bicoronal scalp incision, the scalp flap was reflected to the level of the supraorbital rim. A galea periost flap was prepared and bifrontal craniotomy with cranialization of the frontal sinuses was performed. The sagittal sinus was ligated and cut, the dura and falx cerebri were and flipped basally. After careful elevation of the frontal cortex, the anterior skull base with the remaining tumor mass, olfactory nerves and dorsally up to the optic chiasm is exposed. The tumor mass was resected and the whole tumor-infiltrated sphenoidal plane was exposed. We performed a decompression of the orbital roof as well when necessary to achieve gross total resection (Fig. 1).

3.3. *Skull base reconstruction*

We dissected an autologous galea periost flap, which was then sutured to the basal dura as a patch graft. The patch margins were further reinforced using fibrin/thrombin sealant glue (TISSEEL, Baxter International Inc., U.S.A.) and a fibrin/thrombin sealant matrix (TachoSil, Takeda Pharmaceuticals, Japan) to provide a watertight closure. In three patients, a split graft from the tabula externa was additionally inserted and fixed with titanium miniplates (QuickFlap, Stryker Corporation, U.S.A.) before the galea periost patch was sutured onto the dura (Figs. 2 and 3). This reinforcement procedure was chosen in cases were the bony destruction of the ASB intracranial tumor mass extended up to the middle cranial fossa (Fig. 1).

4. Results

We identified 249 patients that underwent surgical removal of sinonasal malignancies in the observed period. Of those, 11 patients (2 female, 9 male, age (median, SD) 64 $\pm$ 14.1 years (range 38–81) fulfilled the inclusion criteria. Clinical and epidemiological data regarding are depicted in Table 1. All included patients presented with an advanced tumor classification (T4a and T4b). A gross total resection (GTR) according to postoperative MRI and CT imaging was achieved in 9/11 patients. During the median follow-up period of 22.5 $\pm$ 28 months (range: 11–78), tumor relapse was seen in 6 of 11 patients.

Surgery-related complications occurred in 46% (5/11) of all patients (Table 2), requiring early intervention and revision surgery in patients No. 5, 6, and 9. Late surgery due to a chronic nasal CSF fistula was necessary in two patients (18%).

The mortality rate was 55% due to tumor progression or abovementioned complications during the follow-up period.

Table 1

Demographic, histologic and oncologic data. GTR = gross toral resection; RTX = radiotherapy; Gy = Gray; KPS= Karnofsky performance status; post-OP = at dismission from hospital; Status assessed at last follow-up.

Pat. Nr.	Sex	Age at surgery	Diagnosis	Number of previous endoscopic surgeries	Localization	Tumor stage	time from diagnosis to combined surgery (months)	GTR?	Radio-/Chemotherapy	Follow-up (months)	KPS (pre/ post-OP)	Status	PFS (months)	OS (months)
1	m	45	Intestinal-type Adenocarcinoma	1 biopsy, 1 resection	cranio-orbital	T4b	13	yes	docetaxel/cisplatin/5-fluorouracil; gemcitabine/cisplatin/ cetuximab	25	80%/ 80%	dead	22	25
2	m	79	Intestinal-type Adenocarcinoma	0	cranio-naso-orbital	T4a	1	yes	RTX 66 Gy	5	80%/ 60%	dead	4	5
3	m	81	Intestinal-type Adenocarcinoma	1 biopsy, 1 resection	cranio-orbital	T4b	8	yes	RZX 59,4 Gy	62	70%/ 50%	alive	25	62
4	m	79	Poorly-differentiated squamous cell carcinoma	1 biopsy	cranio-naso-orbital	T4a	1	yes	RTX 66Gy, cisplatin + etoposid	64	90%/ 90%	alive	24	64
5	m	77	Olfactory Neuroblastoma Grade II	0	cranio-nasal	T4a	0	no	RTX 66 Gy	78	90%/ 40%	alive	78	78
6	m	62	Intestinal-type Adenocarcinoma	0	cranio-nasal	T4a	1	yes	RTX 64.4 Gy	20	70%/ 60%	dead	14	20
7	m	64	Intestinal-type Adenocarcinoma	0	cranio-nasal	T4a	1	yes	RTX 60 Gy, cisplatin	5	80%/ 80%	dead	5	5
8	w	60	Sinonasal undifferentiated carcinoma	0	cranio-naso-orbital	T4b	0	yes	RTX 64.4 Gy, cisplatin	41	80%/ 70%	alive	41	41
9	m	63	Mucinous Adenocarcinoma	1 biopsy, 1 resection	choanae, frontal sinus	T4a	51	yes	RTX 60 Gy	6	70%/ 30%	dead	6	6
10	w	38	Esthesioneuroblastoma	1 biopsy, 2 resections	cranial- nasal, frontal sinus	T4b	2	no	RTX 66 Gy, cisplatin + etoposid	8	70%/ 70%	dead	4	8
11	m	69	Poorly-differentiated Adenocarcinoma	2 biopsies, 1 resection	cranio-nasal	T4b	2	yes	RTX 66Gy	11	90%/ 90%	alive	11	11

Table 2
Postoperative complications and tumor characteristics.

Pat. No.	Details of complication	Tumor volume pre-OP (cm^3)	Tumor volume post-OP (cm^3)	skull base defect (cm^2)	reoperation?	CSF fistula?	Infection?	severe complication?	primary SB reconstruction?
1	n/a	2.4	0	10.1	no	no	no	no	yes
2	n/a	60	22	7.5	no	no	no	no	no
3	n/a	18.6	0	12.5	no	no	no	no	no
4	n/a	58.1	0	25	no	no	no	no	no
5	subdural empyema, re-craniotomy, evacuation	46.5	0	15	yes	no	yes	no	no
6	fronto-basal CSF fistula, pneumatocephalus, 3 revision surgeries including skull base reconstruction w/ fascia lata, ventriculitis, VP-shunt, lung artery emboly	33.7	5.6	16.2	yes	yes	yes	yes	no
7	rhinoliquorrhoe, revision surgery 4 mo later with skull base reconstruction: galea periost flap	42.4	0	13.4	yes	yes	no	yes	no
8	amaurosis right eye, rhinoliquorrhoe, frontal subgaleal CSF effusion, lumbar drainage for 10 d	35.3	0	15.7	no	yes	no	yes	no
9	pneumatocephalus, 5 d post surgery implantation of right frontal epidural drainage, cerebral infarction left corona radiata and caudate nucleus	27	0	10.5	yes	no	no	yes	yes
10	hydrocephalus malresorptivus, VP-shunt 5 mo after surgery, intracerebral abscess + meningitis, implantation of abscess drainage & explantation of shunt 5 d later	62.4	0	12.3	yes	no	yes	yes	yes
11	n/a	72.7	0	6.1	no	no	no	no	no

5. Discussion

Although the efficacy of chemotherapy and radiotherapy has improved over the years, surgical resection remains the centerpiece of treatment for patients with advanced sinonasal tumors (Guazzo et al., 2019; Castelnuovo et al., 2016). These entities are prone to post-operative complications due to the extent and complexity of the anterior and lateral skull base, impairment of cell proliferation by radiation therapy, and intracerebral invasion. Because advanced sinonasal carcinomas are rare, there is no level I or II evidence for reconstructive surgical approaches.

The main finding of our study is that in patients with extensive tumor growth involving the middle cranial fossa, a tabula externa graft may provide sufficient reinforcement to prevent the occurrence of encephalocele. In addition to the size of the defect, none of these patients had CSF leakage compared to 33% (3/9) of the remaining patients. Frontal lobe drooping, as reported by others after resection of large ASB tumors (Eloy et al., 2012), did not occur. However, pneumatocephalus and communicating hydrocephalus could not be avoided in two of these three patients.

In our series, nine of 11 patients had a skull base defect >10 cm2, suggesting that resection of anterior skull base malignancies results in the loss of a greater proportion of the skull base. The surgical goal can be achieved at the expense of the amount of dura to be resected. A watertight dura closure remains an important goal to prevent secondary complications such as meningitis, pneumocephalus, and CSF leakage through a fistula (Kwon et al., 2012). CSF leakage can occur in 8%–28% of open surgical and endoscopic cases (Eloy et al., 2017; Bohoun et al., 2019; Sokoya et al., 2017). The use of lumbar drainage is controversial. On the one hand, it should help to relieve intracranial pressure at the sites of dural adaptation and closure to facilitate the creation of a closed extra/intracranial barrier. On the other hand, additional CSF drainage may lead to pneumatocephalus as in one of our patients (Ryan et al., 2023; Kwon et al., 2012; He et al., 2021). In our series, every patient received lumbar drainage and pneumatocephalus occurred in 2/11 patients.

Traditionally, sinonasal cancer invading the anterior skull base was treated with craniofacial resection. Over time, endoscopic endonasal techniques have revolutionized surgery for skull base and sinonasal malignancies (Buchmann et al., 2006; Vrionis et al., 2004; Abu-Ghanem et al., 2020). To achieve the maximum extent of resection of skull base tumors, especially those with extensive antero-lateral involvement of the frontal sinus, dural infiltration of the orbital roof, optic chiasm, or brain parenchyma, a combined endoscopic and transcranial approach is recommended (Yong et al., 2021). By combining the endoscopic and open craniotomy approaches, we achieved GTR in 9/11 patients. The disadvantage of extensive resection is a surgical complication rate of 46%, which is consistent with other reports. Here, surgical complication rates of open transcranial reconstruction reach up to 47%, whereas fully endoscopic complication rates occur in up to 29% (Chatelet et al., 2021). Our decision to plan a single surgery rather than a two-stage approach was based on the patients' general health, expected blood loss during surgery, brain swelling, and intracranial tumor extension. Fortunately, there were no perioperative surgical complications leading to termination of the procedure for any of the above reasons. We have summarized the current literature relevant to the specific tumor type and extent of our patient cohort (Table 3). Based on the available publications, our results are favorable despite the aforementioned complications.

Endonasal and extracranial flaps can provide an effective reconstruction that seals and protects the brain parenchyma and CSF from the skull base (Gata et al., 2021). The remaining extensive cranial fossa defect should be reconstructed with a counterpiece, similar to an abutment, to prevent herniation, meningoencephalocele, or osseous erosion due to chronic intracranial pressure exerted on the rim of the resected cavity. There are several options. The defect can be closed with autologous (tabula externa from the patient's frontal craniotomy), allogenic (cadaveric) bone, PEEK or titanium mesh grafts fixed with mini-plates and screws (Eloy et al., 2017; He et al., 2021; Yeung et al., 2021). Disadvantages of autologous grafts are their reabsorption due to continuous brain pulsation, their limited size to cover large defects, or the risk of secondary infection (Eloy et al., 2017; Mohammed-Ali et al., 2013; Bentz et al., 2003; Yong et al., 2016). In general, complication rates of free tissue transfer including bone for anterior skull base reconstruction range from 0% to 67% (Ryan et al., 2023). Bone graft failure, especially

Table 3
Literature overview of selected retrospective studies related to our case series. *Number of patients: patients with diagnosis of meningeoma, osteoblastoma, schwannoma, melanoma, pseudotumors were excluded, total patient number is given in brackets.

Author, year of publication	Recruitment period (years)	Number of patients*	Tumor status (n)	Type of surgery (n)	Complete resection?	Tumor recurrence	Bone graft used?	Surgical complication rate	Follow-up (months)	Mortality	PFS (months)	OS (months)
Buchmann et al., 2006	17	63 (75)	T1 or T2 (22), T3 and T4 (56)	fully endonasal endoscopic (4)/ combined endoscopic sublabial (12)/combined endoscopic, sublabial and craniotomy (20)	63 (T1,T2) and 64% (T3, T4)	35%	no	n/a	39 (SD 40)	17%	41	35
Eloy et al., 2012	1.3	3 (7)	sinunasal carcinoma T4 (3)	fully endonasal endoscopic	n/a	n/a	no	n/a	10 (4–19)	0%	10 (4–19)	10 (4–19)
Guazzo et al., 2019	12	32	T3 (3), T4 (29)	fully endoscopic (7), open (21), combined endoscopic/open (4); craniotomy (9)	31%	9%	no	47%	82 (33–160)	21%	53% (60), 23% (120)	92% (60), 64% (120)
Reinard et al., 2015	18	10 (21)	n/a	craniotomy (10)	n/a	5%	yes	10%	10 (1–99)	0%	n/a	n/a
Mohammed-Ali et al., 2013	6	12 (45)	n/a	cranio-facial open (10)	n/a	n/a	no	46%	12	9%	n/a	12
Bentz et al., 2003	27	72 (166)	T3 and T4	cranio-facial open (72)	n/a	51%	partially	43%	53	n/a	5-year: 41%	5-year: 57%
Yong et al., 2016	7	15 (18)	T3 (5), T4 (13)	subcranial (2), + transorbital (5), + transfacial (5), + midfacial (5), + transorbital endoscopic (1)	33%	17%	no	33%	30 (2–84)	0%	5-year: 40%	5-year: 40%

after postoperative radiation therapy, including aseptic bone necrosis, hardware extrusion, or secondary infection due to CSF leakage, is reported in 5–15% (Garcia-Navarro et al., 2013; Janecka, 2000).

A recent systematic review by Ryan and colleagues provides a practical framework for approaching these anterior skull base lesions (Ryan et al., 2023). According to the algorithmic approach developed by this study group, regional flaps or free tissue transfer are recommended for reconstruction of large ASB defects. Contraindications to free tissue transfer include severe comorbidities, a vascularized neck, coagulopathy, severe obesity, or connective tissue disease. In addition, the choice of regional flap site depends on the localization of previous radiation fields. When defects involve >50% of the ASB, multiple anatomic subsites, or radiation therapy is planned, free tissue transfer appears to be the preferred method of reconstruction.

5.1. Limitations

Due to the small sample size and the retrospective nature of this study, no general recommendation can be drawn from our results. Statistical analysis could not be performed and the group sizes were different, indicating a possible selection bias. Possible confounding factors such as the experience of the neurosurgeon and the otolaryngologist or the watertightness between the layers of the primary dural reconstruction cannot be excluded.

6. Conclusion

In cases of large (>10 cm2) advanced (T4) sinonasal malignancies extending into the middle fossa, structural grafting with bone for ASB reconstruction should be considered. Structural reinforcement may provide an additional aid in preventing CSF leakage. In the context of the current literature, the comprehensive multidisciplinary surgical approach by otolaryngologists and neurosurgeons using endoscopic and open microscopic techniques may lead to promising results despite increased risk and complication rates.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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